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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| 09/470,667 | 12/22/99 | ASAKURA | A 13735(109700 |

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| EXAMINER | |
|---|---|
| WALICKA, M | |
| **ART UNIT** | **PAPER NUMBER** |
| 1652 | 13 |

**DATE MAILED:** 08/28/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. 09/470,667 | Applicant(s) ASAKURA ET AL. | |
|---|---|---|---|
| | Examiner Malgorzata A. Walicka | Art Unit 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *1-3,9 and 17-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-8 and 10-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Relevant pages of the EP 0448969 A2.

The examiner acknowledges Response to Restriction Requirement filed on August 2, 2001, paper No. 12. Applicants elected, with traverse, Group II claims 4-8 and 10-16. In response to the requirement of species election Applicants elected SEQ ID NO:1. Claims 1-28 are pending in the application, claims 4-8 and 10-16, all in part related to SEQ ID NO:1 are subject of this Office action, claims 1-3, 9, 17-28 are withdrawn from consideration as drawn to the nonelected inventions.

## Detailed Office Action

### *1. Election/Restriction*

The Applicants elected, with traverse, Group II drawn to DNA encoding alcohol and aldehyde dehydrogenase (AADH) enzyme, expression vectors, recombinant host, and recombinant production of the enzyme. The traverse pertains to all nine inventions indicated by the examiner.

In the previous restriction requirement the examiner stated that claim 1, 10 and 25 are linking claims. However, upon further review, this was determined to be incorrect. Thus, the examiner withdraws the statement that claim 1 links inventions I and V, claim 10 links inventions II, II, IV, VI and VIII and claim 25 links inventions VII, VIII and IX.

The Applicants arguments have been fully considered and the examiner rejoins Groups III, IV, VI and VIII into a new Group III, claims 17-19, 23-24 and 26-27, drawn to the production of aldehyde, alcohol and carboxylic acid in a fermentor, classified in class 435, subclasses 41, 136, 138, and 148. Also, Groups V, VII, and IX are rejoined into a new Group IV, claims 20-22, 25 and 28, drawn to production of aldehyde, alcohol and carboxylic acid by the enzyme *in vitro*, classified in class 435, subclass 138. For the sake of clarity restriction requirement as redrawn is set forth below.

Group I: claims 1-3 and 9 drawn to an enzyme comprising a recombinant polypeptide having alcohol and aldehyde dehydrogenase activity, classified in class 435, subclass 190.

Group II: claims 4-8, and 10-16, drawn to DNA encoding said enzyme, expression vectors, recombinant host, and recombinant production of the enzyme, classified in class 536, subclasses 23.2, 320.1 and 252.3.

Group III: claims 17-19, 23-24 and 26-27, drawn to production of aldehyde, alcohol, and carboxylic acid in fermentor, classified in class 435, subclasses 41, 136, 138, and 148.

Group IV: claims 20-22, 25 and 28, drawn to production of aldehyde, alcohol and carboxylic acid by the enzyme in vitro, classified in class 435, subclass 138.

Inventions of Group I and II are different for reasons stated in the previous restriction requirement, sent to the Applicants on May 29, 2001.

Inventions of Group I and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are the recombinant enzyme of Group I and methods of production of chemicals, in a fermentor, by transformed organisms of Group III. Inventions I and III have different modes of operation and are not disclosed as capable of use together. Thus, they are distinct.

Inventions of Group I and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product, that is the enzyme of Group I, can be used in a materially different process than that of Group IV, for example for production of antibodies.

Inventions of Group II and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product, DNA encoding the enzyme, expression vectors and recombinant host of Group II can be used to recombinantly produce the enzyme and not for the production of aldehyde, alcohol, and carboxylic acid in a fermentor as claimed in Group III.

Group III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the inventions of Group III and IV relate to different methods of production of the same set of chemicals, the inventions, therefore, cannot be used together.

In their response to the restriction requirement filed on August 29, 2001, paper No. 12, Applicants argue that restriction between Group I, drawn to the AADH enzyme, and Group II should be withdrawn, because the examiner merely concluded the inventions are distinct, by stating that the enzyme may be synthesized chemically, whereas the examiner has not demonstrated the requirement that "the product as claimed can be made by another materially different process..." ( MPEP § 806.05(f), Rev. 1, February 2000, 800-360). The examiner finds this argument not persuasive because the examiner clearly stated that the product could be made by a materially different process, i.e. chemical synthesis. There is no need for a reference explicitly

showing the chemical synthesis of the claimed product. The ordinary artisan would be well aware of available art presenting established techniques of the chemical synthesis of polypeptides.

The applicants also states that Groups I and II are not distinct and therefore do not require a separate search in the patent literature and publications. This is not found persuasive because while the searches for the two Groups overlap, they are not coextensive. The search for Group I would require the search of classes and subclasses unnecessary for the search of elected Group II. For example, search of Group I would require search of class 435, subclass 190 and search of Group II would require search of class 536 subclass 23.2, 320.1 and 252.3

The requirement of election is still deemed proper and is therefore made FINAL.

The examiner acknowledges the election of Group II and SEQ ID NO:1. Claims 4-8 and 10-16, all in part related to SEQ ID NO:1 are subject of this Office action; claims 1-3, 9, 17-28 are withdrawn from consideration as drawn to the nonelected inventions.

## *2. Objections*

This application has been filed with informal drawings, which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

## *3. Rejections*

### *3.1. 35 USC 112, first paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 4-7 and 10-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 4-7 and 10-16 are drawn to DNA molecules encoding a recombinant polypeptide comprising SEQ ID NO:5 and amino acid sequences which contain addition, insertion, deletion and/or substitution of one or more amino acids residue in SEQ ID NO:5 and vectors host cells and methods of use thereof. The genus of DNAs that comprise the claimed DNA molecules is a large variable genus. The specification discloses the sequence of the species encoding enzyme A (SEQ ID NO:1) and schematically presents DNA sequences encoding chimeric enzymes sA2, sA21, sA22,

sB, A/B1, A/B3, B/A1, B/A2 and B/A3 that contain fragments of SEQ ID NO:5 and 6 and have the AADH activity. However, the disclosure does not set forth DNA molecules encoding recombinant polypeptides having a sequence comprising SEQ ID NO:5 and any number of amino acid sequences which contain addition, insertion, deletion and/or substitution of one or more amino acids residue in SEQ ID NO:5. No description has been provided of the recombinant polypeptide sequences encompassed by the claims. No information, beyond the characterization of SEQ ID NO:5 has been provided by Applicants, which would indicate that they had possession of the claimed genus of DNAs encoding the recombinant polypeptides. The specification does not contain any disclosure of the function of all the recombinant polypeptide sequence derived from SEQ ID NO:5 that are within the scope of claimed genus. The genus of claimed recombinant polypeptides is a large variable genus including polypeptides which can have a wide variety of functions. Therefore, many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification does not provide information sufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that Applicants had possession of claimed invention at the time the instant application was filled.

Claims 4-7 and 10-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the DNA molecule of SEQ ID NO:1, or DNA encoding SEQ ID NO:5, and chimeric genes thereof, does not reasonably provide enablement for DNA constructs encoding an AADH activity and comprising at least one sequence of SEQ ID NO:1 and any number of sequences produced by addition, insertion, deletion and/or substitution of one or more nucleotides in SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are so broad as to encompass any DNA encoding an AADH including SEQ ID NO:1 and any number of sequences which are produced by an addition, insertion deletion and/or substitution of one or more nucleotides in SEQ ID NO:1 when the construct encodes a recombinant polypeptide having an AADH activity. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA constructs broadly encompassed by the claims. The specification provides for expressing vectors comprising SEQ ID NO:1 and chimeric genes consisting of different fragments of SEQ ID NO:1 and 2, that encode a functional AADH, yet it does not provide for extremely large number of DNAs that comprise any variant of SEQ ID NO:1 containing addition, insertion deletion and/or substitution of one or more nucleotides. Since DNA sequence determines the amino acid sequence of a protein, predictability of which changes in the DNA of SEQ ID NO:1 can be tolerated to preserve the AADH activity of the mutated encoded protein requires a knowledge of and guidance with regard to which codons of SEQ ID NO:1 if any, are

tolerant of modification and which are conserved (i.e. expectedly intolerant to modification).

While recombinant and mutagenesis techniques are known, it is not a routine in the art to screen enzymatic activity of unlimited number of recombinant polypeptides encoded by DNA constructs containing at least one polynucleotide of unmutated sequences in combination with any number of mutants of this sequence produced by one or more substitutions, insertions and/or deletions of nucleotide in any position.

The specification does not support the broad scope of the claims that encompass unlimited number of DNAs. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including DNA comprising any variant of SEQ ID NO:1 with any number of mutations of this sequence produced by one or more substitutions, insertions and/or deletions to any position. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination which of DNAs will encode a polypeptide retaining the AADH activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The invention appears to employ a new DNA construct, a recombinant expression vector pSSA102R containing SEQ ID NO:1. Since the pSSA102R vector is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed vector sequences are not fully disclosed, nor have all sequences required for the vector construction been shown to be publicly known and freely available. The specification does not disclose a repeatable process to obtain the vector and it is not apparent if the DNA sequences are readily available to the public. Accordingly, it is deemed that a deposit of this vector should have been made in accordance with 37 CRF 1.801-1.809.

If the deposit was made under the terms of the Budapest treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific plasmid containing said cDNA insert has been deposited under the Budapest Treaty and that said DNA construct will be irrevocably and without restriction or conditions released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, Applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

3. the deposit will be maintained in public repository for a period of 30 years or five years after the last request or for the effective life of the patent, whichever is longer: and

4. the deposit will be replaced if it should ever become inviable.

3.2. 35 USC section 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4, 6, 7 and 16 and dependent claims 5 and 10-15 are rejected under 35 U.S.C. 102(b) as being anticipated by EP448969-A entitled "*A. altocetigenes* membrane bound ADH 72 kD sub-unit" issued on October 2, 1991 to Tamaki et al. The patent discloses a gene (SEQ ID NO:1) for membrane-bound alcohol dehydrogenase (SEQ ID NO:3) obtained from *Acetobacter altocetigenes* MH-24 used for production of enzyme for converting alcohol to acid. The sequence of the gene has 2217 nucleotides and 55 % best local similarity to SEQ ID NO:1 of the instant application. Thus the gene disclosed in the patent anticipates the DNA of SEQ ID NO:1 of the instant application with one or more nucleotides added, deleted and/or substituted as claimed in claims 4, 5 and 6. The gene encodes the protein of 739 amino acids with the best local similarity of 28% to SEQ ID NO:5 of the instant application. Tamaki et al further teach vectors ( claim 7), host cells including genus *Acetobacter* and *Gluconobacter* (claims 10-15) and expression of the encoded alcohol dehydrogenase (claim16).

***3. Allowable subject matter***

Claim 8 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, first paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Claim 8 is directed to the pSSA102R vector expressing SEQ ID NO:1. The DNA molecule of SEQ ID NO:1 encodes a novel alcohol and/or aldehyde dehydrogenase of amino acid of SEQ ID NO:5.

As allowable subject matter has been indicated, applicant's reply must either comply with all formal requirements or specifically traverse each requirement not complied with. See 37 CFR 1.111(b) and MPEP § 707.07(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

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